

Surgery for Acquired Cardiovascular Disease

Reoperation is not an independent predictor of mortality during aortic valve surgery

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Objective: Reoperations on aortic valves are associated with increased mortality, which may affect valve prosthesis selection at the time of initial aortic valve replacement. We analyzed our experience to determine whether reoperation itself independently predicts mortality during aortic valve surgery.

Methods: Demographic, intraoperative, and outcome data were collected prospectively on patients undergoing primary or redo aortic valve replacement or Bentall procedures after previous aortic valve replacement with or without concomitant coronary bypass grafting at a single institution from 1990 through 2002. Logistic regression analyses validated by means of bootstrap methodology identified the predictors of hospital mortality and the independent effect of reoperation.

Results: Of 2673 patients undergoing aortic valve surgery, 2375 were primary operations, 216 were reoperations, and 82 were Bentall–after–aortic valve replacement procedures. Of 298 reoperations, 32 were third and 5 were fourth procedures. Mortality was 2.3% for primary operations, 4.6% for redo aortic valve replacement, and 2.4% for Bentall–after–aortic valve replacement procedures. Most patients underwent elective procedures, with mortalities of 1.6%, 1.7%, and 2.5%, respectively. Hospital mortality was independently predicted by peripheral vascular disease (odds ratio, 3.6), active endocarditis (odds ratio, 2.9), worsening New York Heart Association class (odds ratio, 2.3), and need for annular enlargement (odds ratio, 2.1). Reoperation itself did not predict hospital mortality.

Conclusions: The risk of mortality during aortic valve surgery is due mostly to active endocarditis, New York Heart Association class, and comorbidity. We failed to find a significant effect of reoperation on perioperative mortality. Mechanical valves, with their attendant anticoagulation-related morbidity, should not be implanted solely because of anticipated high mortality associated with bioprosthetic rereplacement.

Reoperative aortic valve surgery has traditionally been associated with significant mortality and morbidity.¹ Mechanical valves have a long record of excellent durability² but significant morbidity and sometimes mortality related to anticoagulant-related hemorrhage and other factors.^{3–5} Bioprosthetic aortic valves have excellent freedom from thromboembolism^{3,4} but are subject to primary tissue failure and may therefore require rereplacement.^{6,7}

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Abbreviations and Acronyms

AVR	= aortic valve replacement
CABG	= coronary artery bypass grafting
CI	= confidence interval
LV	= left ventricular
LVEF	= left ventricular ejection fraction
NYHA	= New York Heart Association

Factors like advanced age, left ventricular (LV) dysfunction, and an acute presentation with structural valve failure or infective endocarditis may make reoperations on the aortic valve a challenging proposition. Scarring, distortion, and calcification of the aortic annulus and root present increased technical difficulties, which may require reconstruction of the aortic root. However, because surgical results have improved over time, reoperations on the aortic valve may no longer carry the same increase in risks as in the past. We therefore evaluated our experience with aortic valve surgery to determine whether redo aortic valve replacement (AVR) or Bentall-after-AVR procedures are independent predictors of perioperative mortality.

Methods**Data Source**

From January 1990 through December 2002, 2673 patients underwent AVR with or without concomitant coronary artery bypass grafting (CABG) at our institution. Of these, 2375 patients underwent primary (first-time) AVR, and 298 patients (11.1%) underwent redo aortic valve surgery. Clinical, operative, and outcome data were collected prospectively in a computerized database on all patients undergoing cardiac surgery. Patients who underwent operations on other valves, ventricular aneurysm resection, arrhythmia surgery, or extracardiac procedures were excluded from this study.

Outcome and Explanatory Variables

Our primary outcome in this study was hospital mortality, which was defined as any postoperative death in the hospital. We also recorded age, sex, LV grade (based on left ventricular ejection fraction [LVEF] obtained by means of ventriculography or echocardiography as follows: grade 1, LVEF $\geq 60\%$; grade 2, LVEF 40%-59%; grade 3, LVEF 20%-39%; grade 4, LVEF $< 20\%$), previous AVR, urgency of operation (elective; semiurgent, indicating an operation during the same admission as a cardiac catheterization or a cardiac event; urgent, indicating an operation within 72 hours of an event; or emergency, indicating an operation within 12 hours of an event), New York Heart Association (NYHA) class, native and prosthetic aortic valve lesion (stenotic, regurgitant, or mixed, as determined by means of echocardiography) and infective endocarditis (active endocarditis, active endocarditis with abscess formation, remote endocarditis, or none), recent (within 30 days) myocardial infarction, congestive heart failure, diabetes, hyperlipidemia, peripheral vascular disease, hypertension, and preoperative stroke or transient ischemic attack.

Analysis

Statistical analyses were performed with SAS (Version 8.2) software.⁸ Univariate analyses were performed with χ^2 analyses or the Fisher exact test for categorical variables and analysis of variance for continuous variables. Variables that had a univariate *P* value of less than .25 or those judged to be clinically important were submitted to a logistic regression model by means of stepwise selection. Multivariate logistic regression methods, validated by means of bootstrap methodology, were used to calculate factor-adjusted odds ratios. Model discrimination was evaluated by using the area under the receiver operating characteristic curve,^{9,10} and calibration was assessed with the Hosmer-Lemeshow goodness-of-fit statistic.

Results**Demographics**

Two thousand three hundred seventy-five (88.9%) patients underwent first-time AVR (primary AVR), 216 (8.1%) patients underwent an aortic valve rereplacement (redo AVR), and 82 (3.1%) patients underwent a modified Bentall procedure or complete aortic root replacement with reimplantation of coronary buttons after a previous AVR (Bentall-after-AVR, Table 1). For patients in the redo AVR group, the median duration between operations was 10.3 years (mean, 10.6 ± 5.4 years). For patients in the Bentall-after-AVR group, the median duration was 11.2 years (mean, 11.0 ± 6.2 years).

Patients undergoing reoperations were younger than those undergoing primary AVR ($P < .0001$, Table E1). Patients in the primary AVR group had predominantly aortic stenosis, whereas patients in the redo AVR and Bentall-after-AVR groups had predominantly aortic regurgitation ($P < .0001$). Infective endocarditis and the need for urgent or emergency operation were more common in the redo AVR and Bentall-after-AVR groups ($P < .0001$).

Valvular Pathology

Eighty-three percent of patients in the redo AVR group and 71% in the Bentall-after-AVR group had received a bioprosthetic valve during their previous operation. Most explanted bioprostheses demonstrated cusp tears, calcification, and/or fusion, with many showing pannus ingrowth (Figure 1). Seventeen percent of patients in the redo AVR group and 29% in the Bentall-after-AVR group had received a mechanical valve during their previous operation. Most pa-

TABLE 1. Number of previous aortic valve operations in patients undergoing redo operations

No. of operations	Redo AVR (n)	Bentall-after-AVR (n)
Second operation	191	70
Third operation	23	9
Fourth operation	2	3
Fifth operation	0	1

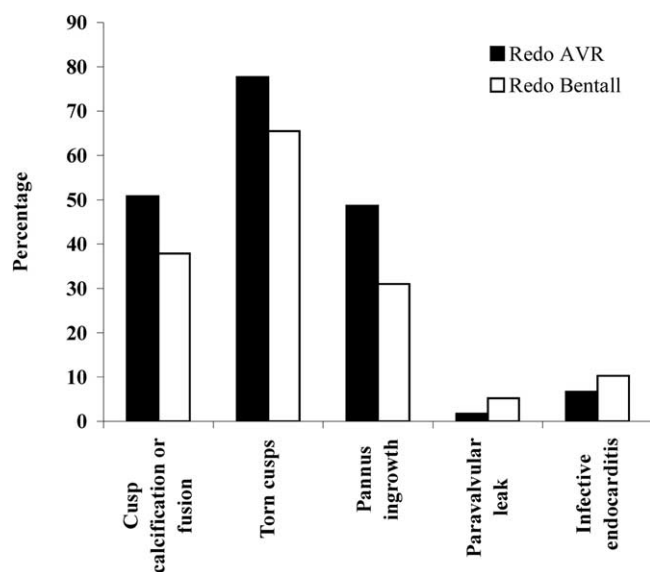


Figure 1. Pathology of explanted bioprosthetic valves. AVR, Aortic valve replacement.

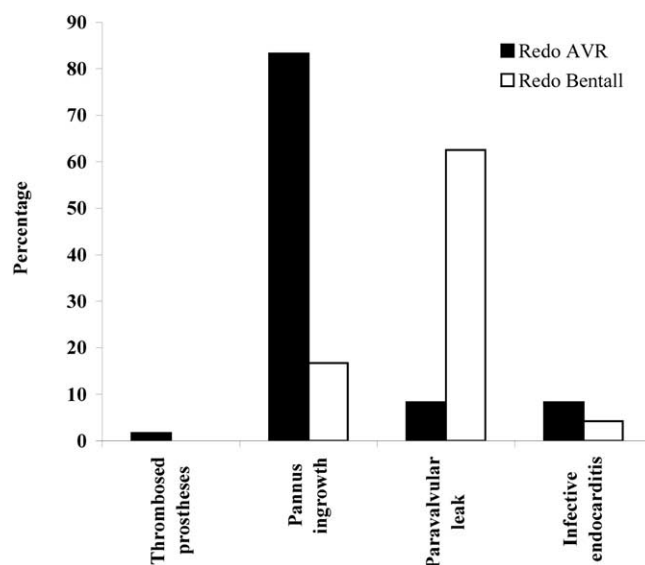


Figure 2. Pathology of explanted mechanical valves. AVR, Aortic valve replacement.

tients in the redo AVR group had significant pannus ingrowth, whereas patients undergoing Bentall-after-AVR procedures chiefly had paravalvular leaks or dehiscences (Figure 2). One valve in the redo AVR group and 11 in the Bentall-after-AVR group were found to be normal at pathologic review. These patients required reoperation predominantly because of abnormalities of the aortic root or proximal ascending aorta.

Of the 82 patients in the Bentall-after-AVR group, the indication for a root replacement was a type A acute or chronic dissection in 10% of patients, dilation of the aortic root in 20%, ascending aortic aneurysm in 12%, periannular abscess in 18%, partial or complete excision of the annulus during excision of the prosthesis in 16%, and a calcified, friable, or abnormal aortic root in 20%. Seven patients undergoing Bentall-after-AVR procedures had a Dacron or pericardial patch enlargement or reconstruction of the aortic root at the time of the previous operation.

Sixteen patients who had undergone primary AVR with Toronto SPV bioprostheses required a reoperation. Eight underwent a redo AVR, and 8 underwent a modified Bentall or root replacement procedure. Eight patients who had undergone primary AVR with a homograft required a reoperation. One patient underwent a redo AVR, and 7 underwent a modified Bentall or root replacement procedure. There were 2 more patients (one with a previous Medtronic Freestyle valve in situ and the other who had undergone a Ross procedure) who underwent redo AVR. Other commonly explanted tissue valves were Carpentier Edwards Porcine, Ionescu-Shiley, and Hancock II Porcine valves

(24%, 21%, and 20% of all tissue valves explanted, respectively).

Intraoperative Data

The proportion of patients who received mechanical valves was significantly higher in the redo AVR and Bentall-after-AVR groups than in the primary AVR group ($P < 0.0001$, Table 2). A greater percentage of patients in the redo AVR group required enlargement of the aortic annulus or one of the sinuses ($P < .05$). Aortic crossclamp and cardiopulmonary bypass times were longer in patients in the Bentall-after-AVR group ($P < .0001$).

Outcomes

Hospital mortality was 2.3% for primary AVR, 4.6% for redo AVR, and 2.4% for Bentall-after-AVR (Table 3). In the redo AVR group, mortality was 3.7% for second operations, 13% for third operations, and 0% for fourth operations. In the Bentall-after-AVR group mortality was 2.9% for second operations and 0% for third, fourth, or fifth operations.

Univariate analyses showed that mortality was high in patients undergoing emergency primary or redo AVR (Table E2). Preoperative cardiogenic shock and congestive heart failure increased mortality to a greater degree for redo AVR than for primary AVR. In all groups the presence of diabetes or active endocarditis or the requirement for patch enlargement of the aortic root were associated with increased mortality. Peripheral vascular disease and preoperative renal failure increased mortality for primary or redo AVR but not for Bentall-after-AVR.

TABLE 2. Distribution of intraoperative variables

Variable	Primary AVR	Redo AVR	Bentall-after-AVR	P value
Valve type (%)				
Mechanical	24	52	61	<.0001
Bioprostheses	76	48	39	
Prosthesis size (diameter in mm)	24 ± 2.3	24 ± 2.2	26 ± 2	<.0001
Annular enlargement (%)				
Annulus	11	19	6.3	<.0001
Sinuses	3.4	3.9	0	
Both	5.4	13	0	
Total	20	36	6.3	
Duration of CPB (min)	110 ± 37	112 ± 45	152 ± 60	<.0001
Duration of XCL (min)	85 ± 29	83 ± 33	117 ± 42	<.0001

AVR, Aortic valve replacement; CPB, cardiopulmonary bypass; XCL, aortic crossclamp.

Postoperative low cardiac output syndrome, myocardial infarction, or stroke did not differ between groups (Table 3), but postoperative renal failure was more common after reoperations ($P = .04$), as were re-exploration for bleeding ($P < .0001$) and permanent pacemaker insertion ($P = .02$). The durations of intensive care unit and hospital stay were longer in patients undergoing reoperations ($P = .02$).

Predictors of Hospital Mortality for Aortic Valve Operations and Reoperations

The independent predictors of mortality were determined by multivariable logistic regression analysis (Figure 3) and included increasing NYHA class (odds ratio, 2.3; 95% confidence interval [CI], 1.5-3.4), infective endocarditis (odds ratio, 2.9; 95% CI, 1.4-5.9), peripheral vascular disease (odds ratio, 3.6; 95% CI, 1.9-6.8), and the requirement for aortic root enlargement (odds ratio, 2.1; 95% CI, 1.2-3.7). However, reoperative aortic valve surgery was not a significant predictor of hospital mortality.

When reoperation was forced into the model, its odds ratio (odds ratio, 1.4; 95% CI, 0.7-2.9) was considerably lower than those associated with NYHA class, endocarditis, peripheral vascular disease, and root enlargement ($P = .34$).

The multivariable model for mortality was robust, with an area under the receiver operating characteristic curve of 0.735 and a Hosmer-Lemeshow goodness-of-fit P value of .7, indicating good model calibration and discrimination. We further validated the model with bootstrap methodology (Table 4). The logistic regression analysis was repeated 100 times in subsets of 2000 patients randomly selected from the entire dataset for each analysis, with replacement. There was excellent correlation of the predictors selected in the 100 bootstrap analyses with those identified in the original model. As Table 4 indicates, NYHA class was identified as a significant predictor of mortality in 98% of these multivariable models and peripheral vascular disease in 96%, but only 4% of models identified reoperation as a predictor. The finding that reoperation was not a significant predictor of hospital mortality was therefore robust.

Discussion

Reoperative valvular surgery is often performed in higher-risk patients rather than those undergoing primary procedures and is more technically demanding. Reoperative aor-

TABLE 3. Distribution of postoperative outcomes

Variable	Primary AVR	Redo AVR	Bentall-after-AVR	P value
Mortality (%)	2.3	4.6	2.4	.1
Low output syndrome (%)	5.7	4.6	7.3	.7
Postoperative MI (%)	1.6	0.9	0	.4
Postoperative stroke (%)	2.4	4.6	2.4	.1
Postoperative renal failure (%)	2.1	4.2	4.9	.04
Pacemaker insertion (%)	5.6	14	26	<.0001
Reopening for bleeding (%)	4.3	6.9	9.8	.02
Duration of ventilation (h)	19 ± 41	25 ± 52	26 ± 77	.1
Duration of ICU stay (h)	54 ± 71	61 ± 63	74 ± 106	.02
Postoperative hospital stay (d)	10 ± 7.4	11 ± 8.1	12 ± 9.4	.02

AVR, Aortic valve replacement; MI, myocardial infarction; ICU, intensive care unit.

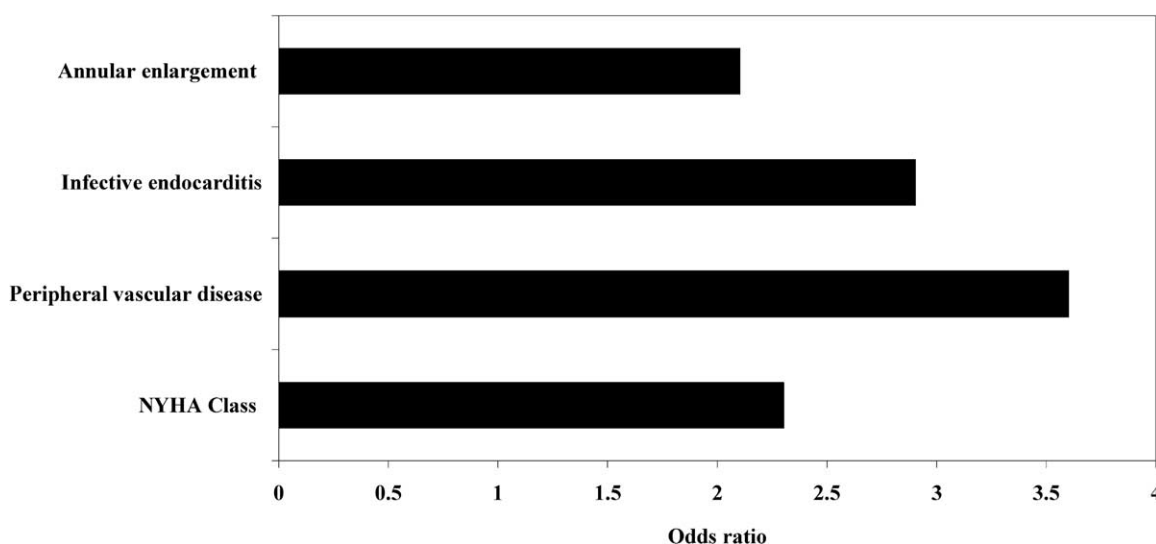


Figure 3. Independent predictors of hospital mortality for primary or redo aortic valve replacement. NYHA, New York Heart Association.

tic valvular surgery after previous AVR¹ or CABG¹¹ has therefore been associated with increased morbidity and mortality compared with that seen with primary procedures. Although some series have reported that prior CABG is not a significant risk factor for mortality during subsequent AVR,^{12,13} the incremental risk of aortic valvular reoperation caused specifically by prior aortic valve surgery has been difficult to quantify.

The desire to avoid subsequent high-risk reoperations may encourage the implantation of mechanical valves because late freedom from structural failure is excellent.²

However, mechanical valves are subject to endocarditis and paravalvular leaks, similar to bioprostheses, and valve thrombosis and pannus ingrowth are not infrequent causes for reoperation. Primary tissue failure is therefore the only indication for reoperation that is specific to bioprostheses. The risk of reoperation for bioprosthetic tissue failure varies by patient age, with excellent valve durability in patients aged 65 years or older.^{6,7,14-16} The likelihood of reoperation for bioprosthetic failure may also be reduced by coronary artery disease, which represents a competing risk.¹⁴ Bioprosthetic aortic valves typically

TABLE 4. Bootstrap analysis for validation of the multivariate regression model

Variable	% of models	Parameter	Standard error	Odds ratio
NYHA class	98	0.7903631	0.0124215	2.2
Peripheral vascular disease	96	1.2879542	0.0194414	3.6
Infective endocarditis	75	1.2537879	0.0239282	3.5
Aortic annular enlargement	61	0.8360244	0.0138950	2.3
Age	16	0.0360655	0.0010653	—
Preoperative MI	16	1.2122562	0.0168738	—
Cardiogenic shock	16	1.3625971	0.0568888	—
Diabetes	12	0.8160644	0.0168738	—
Congestive heart failure	10	0.9471899	0.0373594	—
Syncope-TIA	9	−1.3107508	0.0769650	—
Preoperative renal failure	7	1.3496172	0.0372488	—
Redo vs primary AVR	4	0.9060861	0.0327348	—
Angina	1	−0.7874441	—	—
Hyperlipidemia	0	—	—	—
Sex	0	—	—	—
Preoperative stroke	0	—	—	—

NYHA, New York Heart Association; MI, myocardial infarction; TIA, transient ischemic attack; AVR, aortic valve replacement.

fail gradually, with an increasing incidence of reoperation beginning after 7 to 8 years. In our series we noted median intervals of 10.3 years between operations in the redo AVR group and 11.2 years in the Bentall-after-AVR group, which are very similar to those reported by Vogt and colleagues.¹⁷

When aortic valvular rereplacement was carried out electively, mortality in our series was low (1.6% for elective primary AVR vs 1.7% for elective redo AVR). Vogt and colleagues¹⁷ noted a similarly low risk (1.4%) of elective rereplacement of degenerated aortic bioprostheses, and Akins and associates¹⁸ reported a 4.8% mortality in similar patients. Jamieson and coworkers¹⁹ reported an overall mortality of 6.8% in 322 reoperations for failed aortic bioprostheses.

In the current series reoperative surgery was associated with a nonsignificantly increased risk of mortality (4.6% vs 2.3%). This difference may be due to the increased prevalence of other risk factors in patients undergoing reoperations. For instance, patients presenting with active endocarditis underwent urgent or emergency operations more often in the redo AVR (10.8%) and Bentall-after-AVR (9.1%) groups than in the group undergoing primary AVR (6.4%). Timing of the operation is important because nonelective operation was also reported to be a predictor of death by Akins and associates,¹⁸ with an odds ratio of 2.5.

We also found that worsening NYHA class was a significant predictor of hospital mortality, as did Jamieson and coworkers.¹⁹ Reoperations may therefore involve greater risk not just because of increased technical difficulties but also because such patients often present urgently with endocarditis, congestive heart failure, or shock or with renal failure related to sepsis. These conclusions were also reached by Potter and colleagues,²⁰ who recently analyzed their institutional experience with reoperative aortic valve surgery and concluded that mortality was related to endocarditis, advanced NYHA symptom class, peripheral vascular disease, preserved LV function, and male sex but not to reoperation itself.

In this series an aggressive institutional practice of annular enlargement was reflected in a prevalence of annular enlargement of 20% in patients undergoing primary operations, 36% in patients undergoing redo AVR, and 6% in patients undergoing Bentall procedures after prior AVR. The nominal mean size of valve implanted at reoperation was identical in patients undergoing primary AVR versus redo AVR, whereas those undergoing Bentall procedures received valves with larger sizes. It is likely that without the greater prevalence of annular enlargement during redo AVR, the mean size of prostheses reimplanted would have been significantly lower. The requirement for annular enlargement was associated, however, with a significant increase in hospital mortality. Whether an increased operative

risk caused by annular enlargement is counterbalanced by improved late survival related to a larger prosthesis and improved hemodynamics remains controversial and cannot be addressed by our current study.

Of the 298 patients who underwent reoperations, 82 patients required a Bentall procedure or aortic root replacement for acute or chronic aortic dissections, aneurysmal disease of the aortic root or ascending aorta, annular or subannular abscess cavities, excision of the annulus with the prosthesis, or a calcified or friable aortic root. Patients in this group were younger but had a higher prevalence of active and remote endocarditis and thus required more emergency procedures. Despite this, the overall hospital mortality for this group of patients was only 2.4%, which compares favorably with the 11.5% mortality reported by Valley and associates²¹ for elective root replacement after previous AVR and the 8.3% mortality noted by Dougenis and coworkers²² for root replacement after prior AVR or CABG. We attribute the low mortality in this series to a number of factors, including concentration of cases to a small number of experienced surgeons, ensuring safe sternal reentry, careful myocardial protection, aggressive debridement of all suspicious infected tissues, and reconstruction of the heart with pericardium in patients with aortic root abscesses.²³

Because aortic bioprostheses do not require anticoagulation with warfarin, they are indicated in young patients whose physical activity increases the risk of anticoagulant-related hemorrhage, women who wish to bear children,²⁴ and those in whom anticoagulation cannot be safely monitored and maintained. They are also indicated in elderly patients undergoing AVR (>65 years of age) because of excellent durability and limited patient life expectancy. In addition, some middle-aged patients (40-65 years) choose bioprosthetic valves because of the desire to avoid warfarin therapy. Our results suggest that the median interval between operations and the time course over which symptoms of bioprosthetic tissue failure develop might support this approach in carefully selected patients. When reoperation to replace a failing tissue valve can be carried out on an elective basis, the associated mortality is low.

The strategy of increased use of bioprosthetic valves must be tempered by other mitigating factors. Patients who already have another indication for lifelong warfarin anticoagulation usually have a mechanical valve implanted. In addition, in patients with a small annulus at the time of the initial operation, the necessity of an annular enlargement procedure at future reoperation might be anticipated to be greater, thereby increasing the mortality of reoperation. A mechanical prosthesis, stentless bioprosthesis, or composite root replacement may be better choices for such patients. However, reoperations in patients who have undergone previous stentless valve implantation or root replacement may

be technically more complex. Because patients who underwent aortic root replacement at their initial operation were not included in this series, we are unable to comment on mortality at reoperation in this more challenging patient subgroup.

In conclusion, our experience suggests that the mortality of AVR is strongly related to peripheral vascular disease, endocarditis, NYHA symptom class, and the requirement for annular enlargement. Reoperation itself is not significantly associated with mortality. Bioprostheses implanted to avoid anticoagulation can often be replaced electively with low mortality. Although bioprostheses are not indicated in all patients, the anticipated risk of reoperation may be a less significant consideration in preoperative valve selection in the future.

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TABLE E1. Distribution of preoperative variables

Variable	Primary AVR	Redo AVR	Bentall-after-AVR	P value
No. of patients (n)	2375	216	82	
Age (y)	65 ± 13	59 ± 14	56 ± 15	<.0001
Sex (%)				
Male	67	72	79	.02
Female	33	28	21	
NYHA class (%)				
I	4.4	5.1	15	<.0001
II	23	17	23	
III	46	44	24	
IV	26	33	38	
Diabetes mellitus (%)	16	8.8	11	
Hypertension (%)	44	41	40	
Hyperlipidemia (%)	31	20	22	
Aortic valve prosthesis lesion (%)				
Stenosis	67	13	5.3	<.0001
Regurgitation	14	60	64	
Mixed	19	26	25	
Infective endocarditis (%)				
Active	1.9	3.3	1.2	<.0001
Active, with abscess	0.5	4.2	8.5	
Remote	1.6	9.9	17	
Preoperative cardiogenic shock (%)	3.1	1.4	0	.1
Congestive heart failure (%)	52	73	43	<.0001
Preoperative syncope (%)	20	7.9	2.4	<.0001
Left ventricular ejection fraction (%)				
≥60	43	32	23	.0009
40-59	40	48	59	
20-39	15	17	17	
<20	2.2	3.2	1.2	
Preoperative stroke (%)	10	18	15	.002
Peripheral vascular disease (%)	8.5	6	2.4	.07
CABG (%)	46	31	29	<.0001
Urgency of operation (%)				
Elective	69	54	49	<.0001
Same hospitalization	24	30	27	
Urgent	6.2	13	17	
Emergency	1.1	2.8	7.3	

AVR, Aortic valve replacement; NYHA, New York Heart Association; CABG, coronary artery bypass grafting.

TABLE E2. Influence of preoperative and intraoperative variables on hospital mortality by univariate analysis

Variable	Primary AVR	Redo AVR	Bentall-after-AVR
No. of procedures (%)			
1	2.3 (54/2375)	NA	NA
2	NA	3.7 (7/191)	2.9 (2/70)
3	NA	13 (3/23)	0 (0/9)
4	NA	0 (0/2)	0 (0/3)
Urgency of operation (%)			
Elective	1.6	1.7	2.5
Same hospitalization	3.2	9.2	0
Urgent	2.7	3.6	7.1
Emergency	22	17	0
<i>P</i> value	<.0001	.06	.6
Preoperative cardiogenic shock (%)			
Yes	8.2	33	NA
No	2.1	4.2	
<i>P</i> value	.0005	.02	
Congestive heart failure (%)			
Yes	3.2	6.4	2.9
No	1.2	0	2.1
<i>P</i> value	.001	.04	.8
Infective endocarditis (%)			
None or remote	2.1	3.4	0
Active or active with abscess	6.4	11	9.1
<i>P</i> value	.07	.05	.02
Left ventricular ejection fraction (%)			
≥60	1.9	4.4	0
40-59	1.9	4.9	2.1
20-39	4.3	5.4	7.1
<20	1.9	0	0
<i>P</i> value	.05	.9	.6
Diabetes			
Yes	4.5	5.3	11
No	1.9	4.6	1.4
<i>P</i> value	.002	.9	.07
Peripheral vascular disease (%)			
Yes	6.4	23	0
No	1.9	3.5	2.5
<i>P</i> value	<.0001	.001	.8
Preoperative renal failure (%)			
Yes	6.1	22	0
No	2.2	3.9	2.6
<i>P</i> value	.06	.01	
Aortic root enlargement (%)			
Yes	3.5	11	20
No	1.9	1.5	1.3
<i>P</i> value	.03	.003	.01

AVR, Aortic valve replacement; NA, not applicable.